

# PATENT COOPERATION TREATY

From the

INTERNATIONAL SEARCHING AUTHORITY DATE NTD

To:

# PCT

see form PCT/ISA/220

30. MAY 2005

SPS

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2005/000339

International filing date (day/month/year)  
01.02.2005

Priority date (day/month/year)  
05.02.2004

International Patent Classification (IPC) or both national classification and IPC  
C07D495/04, A61K31/519, A61P35/00

Applicant  
ASTRAZENECA AB

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
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International application No.  
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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. II Priority**

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1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

|                               |             |     |
|-------------------------------|-------------|-----|
| Novelty (N)                   | Yes: Claims | 1-9 |
|                               | No: Claims  |     |
| Inventive step (IS)           | Yes: Claims | 1-9 |
|                               | No: Claims  |     |
| Industrial applicability (IA) | Yes: Claims | 1-9 |
|                               | No: Claims  |     |

2. Citations and explanations

**see separate sheet**

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

**see form 210**

AP20 Rec'd PCT/PTO 04 AUG 2006

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000339

**Re Item V****Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement****V-1. State of the art:**

The following documents are considered relevant:

- D1: WO 2004/013141 A (ASTRAZENECA AB; ASTRAZENECA UK LIMITED; LUKE, RICHARD, WILLIAM, ARTHUR) 12 February 2004 (2004-02-12)  
D2: US 2004/014756 A1 (MICHAELIDES MICHAEL R [US] ET AL) 22 January 2004 (2004-01-22)  
D3: WO 03/022852 A (GLAXOSMITHKLINE K.K; SMITHKLINE BEECHAM CORPORATION; ADAMS, JERRY, LER) 20 March 2003 (2003-03-20)  
D4: WO 02/062804 A (PHARMACIA ITALIA S.P.A; BERTA, DANIELA; FELDER, EDUARD; VULPETTI, ANNA) 15 August 2002 (2002-08-15)

D1 is a P-document and will be disregarded during the PCT phase.

**V-2. Novelty (Art. 33(2) PCT):**

Claims 1-9 are novel over D2-D4. The compounds disclosed in D2 and D3 lack the imidazole ring. The compounds of D4 are condensed oxazoles rather than thiophenes and have a pyrazole instead of the imidazole ring.

**V-3. Inventive step (Art. 33(3) PCT):**

The present application deals with angiogenesis inhibitors which act in particular on the Tie2 receptor tyrosine kinase.

The problem to be solved in view of D2 (which is representing the closest state of the art) is the provision of further compounds having this activity. Having regard to the major

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structural differences (see above) this problem has been solved in a non-obvious way.  
Art. 33(3) PCT is thus also fulfilled.

**Re Item VI**

**Certain documents cited**

**Certain published documents**

| Application No<br>Patent No | Publication date<br>(day/month/year) | Filing date<br>(day/month/year) | Priority date (valid claim)<br>(day/month/year) |
|-----------------------------|--------------------------------------|---------------------------------|---|
| WO2004/013141               | 12.02.2004                           | 01.08.2003                      | 06.08.2002                                      |